### WHAT IS LIFE?

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NEURAL PLASTICITY For good and for bad Aage R. Møller University of Texas at Dallas School of Behavioral and Brain Sciences Texas, USA

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### THE BRAIN IS PLASTIC

 The blueprint for the central nervous system is laid down by genetics (and epigenetics), but its organization and function is constantly revised ("MIDCOURSE CORRECTIONS")

## ACTIVATION OF NEURAL PLASTICITY

- Can be beneficial
- Can be harmful, cause diseases (PLASTICITY DISORDERS)
- Is necessary for normal development of the central nervous system

# WHAT IS NEURAL PLASTICITY?

- Neural plasticity is a property of the nervous system that is only apparent when activated
- Plastic changes comprises
  - synaptic efficacy,
  - formation or elimination of synapses, axons and dendrites
  - programmed cell death
- When activated it can
  - change the function of the brain and spinal cord
  - re-direct the flow of information

# WHAT CONTROLS ACTIVATION OF NEURAL PLASTICITY?

- Lack of stimulation of sensory systems
- Stimulation "neurons that fire together wire together" (Hebb, 1949).
- Other environmental factors
- Unknown factors

# BENEFICIAL EFFECT OF ACTIVATION OF NEURAL PLASTICITY

# ACTIVATION OF NEURAL PLASTICITY AFFECTS THE QUALITY OF LIFE

- Benefit:
- Recovery from trauma (stroke)
  Adapt to changing demands
  Harm (*Plasticity disorders*):
  Cause pain (central neuropathic pain)
  Tinnitus (ringing in the ears)
  Hyperactivity of motor functions (spasticity)

ACTIVATION OF NEURAL PLASTICITY CAN HELP *RECOVERY FROM TRAUMA* Make use of redundancy

- Re-route information that has been processed in the damaged parts of the brain to intact parts
- Not all brain functions have redundancy
  - -Speech is exclusively left side of the brain

ACTIVATION OF NEURAL PLASTICITY CAN HELP ADAPTING TO CHANGING DEMANDS

Use of prostheses

- Cochlear and brainstem implants to treat deafness requires reprogramming of hearing
- The use of artificial limbs requires reprogramming of motor control

## **COCHLEAR IMPLANTS**

- Bypasses the frequency selectivity in the cochlea
- Bypasses neural transduction in the hair cells and activate auditory nerve fibers directly
- Bypasses two-tone inhibition
- Bypasses the frequency dependent basilar membrane traveling time

### **GENERAL PRINCIPLE FOR COCHLEAR IMPLANTS**



FROM MØLLER, 2006

THE BASIS FOR MODERN COCHLEAR IMPLANTS THE CHANNEL VOCODER Developed for analysis-synthesis telephony in 1950's

- Provides only spectral information
- Extracts the energy in a few (8-14) frequency bands
- Discards fine temporal information

### "CHANNEL VOCODER" COCHLEAR IMPLANT PROCESSOR



ADDING MORE CHANNELS WAS A MAJOR IMPROVEMENT IN SPEECH DISCRIMINATION

How many channels are needed for good speech discrimination?



The principles of the channel vocoder is similar to that of trichromatic color vision

Only three filters channels provide information about all nuances of color Three pigment system



MOLLER 2006 AFTER SHEPHERD

Place coding alone is sufficient for speech discrimination

Temporal coding alone is sufficient for speech discrimination

The normal auditory system has considerable redundancy

NEURAL PLASTICITY IS NECESSARY FOR THE USE OF COCHLEAR IMPLANTS

The young brain is more malleable than the adult brain

### TIME OF IMPLANTATION IS IMPORTANT

The P1 component of auditory evoked potentials is an objective measure of adaptation to cochlear implants, thus a sign of the plastic changes



From Sharma and Dorman 2006

ACTIVATION OF NEURAL PLASTICITY CAN CAUSE HARM *"PLASTICITY DISORDERS"* 

- Pain (central neural neuropathic pain)
- Severe chronic tinnitus
- Spasm
- Spasticity
- Synkinesis

### ACTIVATION OF NEURAL PLASTICITY INVOLVES A CASCADE OF STRUCTURES



### THIS IS SIMILAR TO OTHER DISORDERS SUCH AS DIABETES TYPE 2







#### **ACUTE PAIN**

#### SPINOTHALAMIC TRACT

CENTRAL PAIN PATHWAYS PROJECT TO PRIMARY CORTICES WITH SPATIAL INFORMATION ("WHERE")

OBJECTIVE INFORMATION ("WHAT") PROJECTS TO MANY DIFFERENT PARTS OF THE CNS (FOR EXAMPLE THE *LIMBIC SYSTEM*)



#### THERE ARE DIFFERENT TYPES OF PAIN



### SOMATIC PAIN From stimulation of pain receptors



## CENTRAL NEUROPATHIC PAIN

Pain that is caused by abnormal neural activity in the brain caused by activation of neural plasticity

### THE DORSAL HORN OF THE SPINAL CORD IN A PATHOLOGIC MODE

Redirect somatosensory information to pain circuits causing allodynia (light touch cause painful sensation)





Sensation of sound in the absence of any physical sound

# TINNITUS IS ASSOCIATED WITH RE-ROUTING OF INFORMATION

Involves non-classical sensory pathways



## **RE-ROUTING OF INFORMATION**



### THE EMOTIONAL BRAIN

Connections between the classical and the non-classical auditory systems and the amygdala involve both the "high route" and the "low route"



From: Møller: Sensory Systems, 2003

EXPOSURE TO LOUD NOISE AND HEARING LOSS CAN CAUSE TINNITUS

Tinnitus is associated with changes in non-auditory parts of the brain

#### **HIPPOCAMPUS:** Normal stable place cells



#### Place-cells are affected after noise exposure



DEPRIVATION OF INPUT CAN GIVE SYMPTOMS OF *PLASTICITY DISORDERS* 

Hyperactivity (tinnitus)Pain



BALANCE DISORDERS An example of re-routing of information

- Awareness of head movement
- Vertigo
  - benign paroxysmal positional nystagmus
  - disabling positional vertigo



Involuntary muscle contractions, often associated with synkinesis (simultaneous contractions of different muscles)

# IRRITATION OF THE FACIAL NERVE ROOT AND HEMIFACIAL SPASM



### CONCLUSION

- Activation of neural plasticity can make information reach other parts of the CNS than normally receive such information
- This may occur by unmasking of dormant synapses or creation of new structures
- This explains why plasticity disorders can be associated with many different kinds of symptoms and sign

NORMAL DEVELOPMENT OF AN INDIVIDUAL ORGANISM DEPENDS ON:

- Genetics (and epigenetics)
- Environmental factors
- Unknown factors

ACTIVATION OF NEURAL PLASTICITY IS NECESSARY FOR NORMAL CHILDHOOD DEVELOPMENT

- Postnatal plastic changes involve a cascade of events in a series of structures
- The events are controlled by a program that most likely is created prenatal



NORMAL CHILDHOOD DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM INVOLVES ACTIVATION OF PLASTICITY

- Apoptosis (programmed cell death)
- Adjustment of synaptic efficacy
- Pruning of axons and dendrites

# POSTNATAL DEVELOPMENT

Plastic changes provide "midcourse correction" of the genetically controlled (Darwinian) development of the nervous system

## DEVELOPMENTAL DISORDERS

Postnatal development going awry: For example: Autism spectrum disorders

## AUTISM

- Problems with social interactions
- Abnormal perception of sensory input
- Symptoms may be associated with abnormal involvement of the amygdala

## **AUTISM**

### • SPECULATION:

- Insufficient postnatal pruning and programmed cell death are involved in autism
  - The amygdala and other brain structures in autistic children have a higher packing density of cells than normal

## **DEVELOPMENTAL DISORDERS**

 The programs that control childhood development may be faulty but symptoms may comes from structures that are normal but receive faulty input



# FACTORS TO CONSIDER WHEN TREATING PLASTICITY DISORDERS

- Abnormal neural activity can be caused by pathology or by receiving abnormal activity
- Neural plasticity is controlled by programs that are of genetic and epigenetic in origin and modified by environmental factors
- Neural plasticity may create bistable neural circuits

# PLASTICITY DISORDERS ARE CHARACTERIZED BY ABNORMAL NEURAL ACTIVITY IN SEVERAL STRUCTURES



WHICH OF THE STRUCTURES THAT HAVE ABNORMAL ACTIVITY SHOULD BE TARGET FOR TREATMENT?

- Pathologic structures: May cure the disorder
- Structures that receive pathologic input: May ameliorate symptoms during treatment
- Bistable structures must be reversed

IN SUMMARY THE BRAIN IS PLASTIC, BENEFICIAL OR HARMFUL

- Expression of neural plasticity provides "mid-course corrections" of genetic programs
- Adapt to changing demands; re-route information to functioning parts of the CNS
- Cause tinnitus and central neuropathic pain
- Cause systems can operate in different modes, being "bistable"

### WHAT IS LIFE ?

IT DEPENDS ON THE OBSERVER (SIX BLIND MEN AND AN ELEPHANT)

> LIFE IS DYNAMIC; FOR GOOD AND FOR BAD

> > LIFE PROVIDES OPPORTUNITIES

#### **THE BRAIN**

#### "I DOUBT, THEREFORE I THINK; THEREFORE I AM"

Descartes 1596-1650



Chick

